

# NOVEL, PROGRAMMABLE NUCLEIC ACID BINDING AND CLEAVING CRISPR PROTEINS WHICH CAN SENSE AND RESPOND TO THE CELLULAR ENVIRONMENT

Tech ID: 25952 / UC Case 2016-195-0

## PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,180,778	11/23/2021	2016-195

## BRIEF DESCRIPTION

RNA-programmed Cas9 has proven to be a versatile tool for genome engineering in multiple cell types and organisms. Guided by a dual-RNA complex or a chimeric single-guide RNA, Cas9 (or variants of Cas9) can generate site-specific double-stranded or single-stranded breaks within target nucleic acids. Target nucleic acids can include double-stranded DNA and single-stranded DNA as well as RNA. When cleavage of a DNA occurs within a cell (e.g., genomic DNA in a eukaryotic cell), the cell can repair the break in the target DNA by non-homologous end joining or homology directed repair. Thus, CRISPR/Cas systems provide a facile means of modifying genomic information. Because the effectiveness of many Cas9 protein fusions is less than optimal (likely due to steric incompatibility), there is a need for variants of RNA-guide polypeptides (e.g., variant Cas9 proteins) that provide for, for example, conditionally active proteins and/or more efficient fusion proteins.

UC Berkeley researchers have created circularly permuted Cas9 proteins (cpCas9 proteins) with entirely new N- and C- termini at defined sites around the Cas9 protein structure. The cpCas9 proteins were found to increase the effectiveness of Cas9 fusion proteins because they reduce the constraints imposed by the naturally existing N- and C-termini. The researchers have shown their RNA-guided polypeptides provide increased target nucleic acid editing accuracy (increased in some cases with single nucleotide resolution). Multiple different cpCas9 proteins were developed, each of which provides new N- and C- termini at unique positions within the structure of the Cas9 protein. Thus, depending on the fusion partner of choice, an appropriate cpCas9 can be selected that will place the fused partner at a desired position. This ability to position a fusion partner relative to the structure of the protein while allowing fusion to an N- and/or C-terminus, provides RNA-guided polypeptides that are better suited to avoid off-target effects.

## SUGGESTED USES

- » RNA-guided polypeptides to sense and respond to cellular inputs (e.g., presence of a protease such as a viral protease), causing a cellular output

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## INVENTORS

- » Savage, David Frank

## OTHER INFORMATION

### KEYWORDS

gene therapy, genetic engineering, CAS9

### CATEGORIZED AS

- » **Biotechnology**
- » Genomics
- » **Medical**
- » Gene Therapy
- » Research Tools

### RELATED CASES

2016-195-0

» Binding and/or modifying a target nucleic acid

## ADVANTAGES

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» RNA-guide polypeptides that provide conditionally active proteins and/or more efficient fusion proteins

## ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ Compression of Genetic Information in Multiple Reading Frames
- ▶ 2'-fluoro RNA Activators for Enhanced Activation of Csm6 in RNA Detection Assays
- ▶ Composition and Methods of a Nuclease Chain Reaction for Nucleic Acid Detection



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